PATENT COOPERATION TRF Y 2026-4303 PC

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From the INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

FEILER, William S. Mo:gan & Finnegan, L.L.P. 345 Park Avenue New York, New York 10154 ETATS-UNIS D'AMERIQUE PCT

NOTIFICATION OF TRANSMITTÂL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing

(day/month/year)

23.10.2001

Applicant's or agent's file reference

International application No.

2026-4303PC

PCT/US00/15527

International filing date (day/month/year)

02/06/2000

Priority date (day/month/year)

04/06/1999

Applicant

NATIONAL INSITUTES OF HEALTH

- 1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
- 2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
- 3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

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PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's	or agent's file reference		See Notific	cation of Transmittal of Interna	tional					
2026-43	03PC	FOR FURTHER ACTIO		y Examination Report (Form P						
Internation	al application No.	International filing date (day/mo	onth/year)	Priority date (day/month/year)						
PCT/US	00/15527	02/06/2000		04/06/1999						
Internation C12N15		r national classification and IPC		·						
Applicant			•							
NATION	AL INSITUTES OF HEA	LTH		<u> </u>						
	international preliminary ex s transmitted to the applica	amination report has been prepa nt according to Article 36.	red by this Inte	ernational Preliminary Exa	mining Authority					
2. This	2. This REPORT consists of a total of 7 sheets, including this cover sheet.									
(☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT). These annexes consist of a total of sheets.									
1	☑ Basis of the report☐ Priority									
111	•	of opinion with regard to povolty	novelty, inventive step and industrial applicability							
IV	□ Non-establishment □ Lack of unity of inve □		inventive step	and mudstrial applicability						
v										
VI	☑ Certain documents	cited								
VII	Certain defects in the	e international application	-							
VIII	☐ Certain observation:	s on the international application								
Date of sub	omission of the demand	Date	of completion of	this report						
02/01/20	02/01/2001			23.10.2001						
	mailing address of the internati examining authority:	onal Autho	orized officer		SE SONES MILITARES					
9)	European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523	Pare	esce, D		The sound of the s					
	Fax: +49 89 2399 - 4465	Talas	hono No 140 0	2200 9005	San Spice Breeze					

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/15527

l. Basis d	of the i	eport
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1.	the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)): Description, pages:								
	1-3	7	as originally filed						
Claims, No.:									
	1-2	1	as originally filed						
	Drawings, sheets:								
	1/1	9-19/19	as originally filed						
	Sequence listing part of the description, pages:								
	.1-3	6, as originally filed							
2.	Wit lang	With regard to the language , all the elements marked above were available or furnished to this Authority in the anguage in which the international application was filed, unless otherwise indicated under this item.							
	The	ese elements were	available or furnished to this Authority in the following language: , which is:						
		the language of a	translation furnished for the purposes of the international search (under Rule 23.1(b)).						
			ublication of the international application (under Rule 48.3(b)).						
		the language of a 55.2 and/or 55.3).	translation furnished for the purposes of international preliminary examination (under Rule						
3.			eleotide and/or amino acid sequence disclosed in the international application, the y examination was carried out on the basis of the sequence listing:						
	×	contained in the in	ternational application in written form.						
	\boxtimes	filed together with	the international application in computer readable form.						
		furnished subsequ	ently to this Authority in written form.						
		furnished subsequ	ently to this Authority in computer readable form.						
			t the subsequently furnished written sequence listing does not go beyond the disclosure in pplication as filed has been furnished.						
		The statement that listing has been fu	t the information recorded in computer readable form is identical to the written sequence rnished.						
4.	The	amendments have	resulted in the cancellation of:						



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International application No. PCT/US00/15527

								•					
		the description,	pages:										
		the claims,	Nos.:										
		the drawings,	sheets:										
5.	5. This report has been established as if (some of) the amendments had not been made, since they have b considered to go beyond the disclosure as filed (Rule 70.2(c)): (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to the report.)												
		report.)	eer comaining st	ICI	'i ai	menaments	must be	, ieieiii	eu lo un	iei ileiii	i anu a	minexe	น เบ แทร
6.	Add	itional observations, i	f necessary:										
IV.	Lac	k of unity of invention	on										
1.	In re	esponse to the invitati	on to restrict or p	ау	/ ad	dditional fees	the app	plicant	has:				
restricted the claims.													
	×	paid additional fees.											
		paid additional fees u	ınder protest.										
		neither restricted nor	paid additional f	ee	s.	•							
2.		This Authority found 68.1, not to invite the							omplied a	and cho	se, acc	ording t	to Rule
3.	This	Authority considers t	hat the requirem	en	it of	f unity of inv	ention in	accor	dance w	th Rules	s 13.1,	13.2 an	d 13.3 i
		complied with.											
		not complied with for	the following rea	ıso	ons:	::							
4.		sequently, the following sequently, the following sequently, the following sequential sequential sequential seq		ter	rnat	tional applic	ation we	ere the	subject (of interna	ational ₍	prelimir	nary
	\boxtimes	all parts.											
•		the parts relating to c	laims Nos										
	cita	soned statement un tions and explanatio					novelty,	, inven	tive step	or indu	ustrial	applica	ıbility;
1.	Stat	ement											
	Nov	Novelty (N) Yes: Claims 1-10, 14-21											



INTERNATIONAL PRELIMINARY **EXAMINATION REPORT**

International application No. PCT/US00/15527

No:

Claims 11-13

Inventive step (IS)

Yes:

Claims 1-10, 14-21

No:

Claims 11-13

Industrial applicability (IA)

Yes:

Claims 1-21

No: Claims

2. Citations and explanations see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet



INTERNATIONAL PRELIMINARY **EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/15527

Lack of unity (Rule 13.1 PCT):

The documents mentioned in this communication are numbered as in the search report, i.e. D1 corresponds to the first document of the search report.

The IPEA agrees with the objection put forward by the Search Division as to lack of unity (Rule 13.1 PCT). The IPEA is also of the opinion that the present set of claims relates to two different inventions (see International Search Report). The separate inventions/groups of invention are:

- 1) Claims 1-6, 11-13 (completely) and 9-10, 14-21 (partially) are directed to a nucleic acid molecule comprising a chimeric virus genome, said genome being a BVDV genome in which the structural region of the BVDV genome has been replaced by the structural region of a hepatitis C virus genome. The claims are further directed to a DNA construct comprising said molecule, an RNA transcript of said DNA construct, a host cell transfected with said DNA construct or RNA construct, a chimeric HCV-BVDV produced by said host cell and a composition comprising said virus.
- 2) Claims 7-8 (completely) and 9-10, 14-21 (partially) are directed to a nucleic acid molecule comprising a chimeric virus genome, said genome being a BVDV genome in which the non-structural region of the BVDV genome has been replaced by the non-structural region of a hepatitis C virus genome. The claims are further directed to a DNA construct comprising said molecule, an RNA transcript of said DNA construct, a host cell transfected with said DNA construct or RNA construct, a chimeric HCV-BVDV produced by said host cell and a composition comprising said virus.

The general inventive concept underlying the two above identified inventions of the present application can be seen as the provision of chimeric BVDV-hepatitis C virus genomes. This general inventive concept, however, is not considered novel because, as illustrated by D1, the concept of providing chimeric BVDV-hepatitis C virus genomes was known in the prior art. In D1, a functional clone of BVDV was used to construct and characterize a series of 5' NTR chimeras with sequences derived from the hepatitis C virus (HCV) as well as other flaviviruses. The results



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of this study help to define the requirements of a functional BVDV 5' NTR and provide replication-competent BVDV-HCV chimeras dependent on a functional HCV internal ribosome entry site (see D1, p. 1419).

In view of D1, the problem underlying the present application is considered as the provision of further BVDV-HCV chimeric genomes. One solution to this problem provides a chimeric virus genome, said genome being a BVDV genome in which the structural region of the BVDV genome has been replaced by the structural region of a hepatitis C virus genome. The second solution is considered the provision of a chimeric virus genome, said genome being a BVDV genome in which the non-structural region of the BVDV genome has been replaced by the non-structural region of a hepatitis C virus genome.

In response to an invitation to pay additional fees (see Form PCT/IPEA/405), the Applicant paid the additional examination fees. Consequently the international preliminary examination will be based on claims 1-21 of the present application.

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Novelty: Article 33(2) PCT 1)

> D1 discloses the construction and characterization of a series of BVDV-hepatitis C virus (HCV) 5' NTR chimeras. The results of this study help to define the requirements of a functional BVDV 5' NTR and provide replication-competent BVDV-HCV chimeras dependent on a functional HCV internal ribosome entry site (see D1, p. 1419).

> D2 discloses chimeric genomes of poliovirus in which the cognate internal ribosomal entry site element was replaced by genetic elements of hepatitis C virus (see abstract).

D3 presents a review of flavivirus research and, in particular, flavivirus vaccines. D3 mentions the development of chimaeric viruses as potential vaccine



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candidates. D3 discloses dengue virus chimeras, TBE/dengue virus chimeras. poliovirus expression vectors and mentions developments in generating RNA viruses from cloned cDNA (see p. 975).

D4 and D5 describe the sequence and structural elements of BVDV (see abstracts).

The subject-matter of claims 11-13 is not considered new in the sense of Article 33(2) PCT for the following reasons: The subject-matter of these claims, when interpreted in the broadest sense possible, covers any polypeptide encoded by a BVDV nucleic acid sequence or a hepatitis C virus nucleic acid sequence. BVDV and hepatitis C virus proteins were known in the prior art at the priority date of the present application (see D1-D5). Therefore, these claims are not considered novel.

D1 discloses BVDV-hepatitis C virus (HCV) chimeras in which the nontranslated regions of the BVDV genome were replaced with those from HCV. D1 does not disclose BVDV-hepatitis C virus (HCV) chimeras in which the structural or nonstructural region of the BVDV genome is replaced with the structural or nonstructural region of the HCV genome. The subject-matter of claims 1-10, 14-21 has not, in fact, been made available to the public by any of the available prior art documents and can therefore be regarded as novel.

The subject-matter of claims 1-10, 14-21 cannot be derived from the available prior art in an obvious manner and therefore complies with the requirements of Article 33(3) PCT.

VI: Certain documents cited

Certain published documents (Rule 70.10)

Application No Patent No

Publication date (day/month/year)

Filing date (day/month/year) Priority date (valid claim) (day/month/year)

WO9955366

04.11.99

23.04.99

24.04.98